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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
STRZELECKA, TERESA E

ART UNIT	PAPER NUMBER
1637	11

DATE MAILED: 01/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/921,645	MEADE ET AL.	
	Examin r	Art Unit	
	Teresa E Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51-79* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51-79* is/are rejected.

7)☒ Claim(s) *51,62,67 and 68* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II (claims 41-50) in Paper No. 10 is acknowledged. The traversal is on the ground(s) that the classification of claims 41-50 in class 435, subclass 94 is improper, since this class is unrelated to detection of target nucleic acids using an array. This is not found persuasive because the proper classification of Group II claims in class 435, subclass 6, is still different than the classification of the claims drawn to an array, classified in class 435, subclass 287.2, therefore the restriction requirement is proper.

The requirement is still deemed proper and is therefore made FINAL.

2. Applicants cancelled claims 15-50 and submitted new claims 54-82, which have been renumbered as 51-79. As these claims are drawn to a method of using the array for hybridization detection, they will all be examined. In addition, Applicants elected the following species for the variables R_1, R_2, SCM, X, Y and n: hydrogen, hydrogen, thiol-containing moiety, hydroxyl, oxygen and 16.

3. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Priority

4. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The second application must be an application for a patent for an invention which is also disclosed in the first application (the parent or provisional application); the disclosure of the invention in the parent application and in the second application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ 2d 1077 (Fed. Cir. 1994).

In particular, Applicants claim priority to three applications: 1) 09/639, 311, filed on 8/15/2000 (U.S. Patent No. 6,291,188); 2) 08/808,750, filed on 2/28/1997 (U.S. Patent No. 6,265,155) and 3) 08/475,051, filed on 6/07/1995 (U.S. Patent No. 5,824,473). Applicants assert that the current application is a continuation of #1, which is a continuation of #2, which is a continuation of #3. However, application #2 is not a continuation of the application #3: the disclosures and the subject matter are different.

Therefore, the current application is entitled to the priority date of the 08/808,750 application, which is February 28, 1997.

Information Disclosure Statement

5. The information disclosure statement filed on March 25, 2002 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, and the information referred to therein has been considered only for the documents provided.

Applicants provided copies of only 18 patents (out of 62 listed), one copy of a foreign patent (out of 27 listed) and copies of two non-patent documents (out of 133 listed).

Specification

6. The disclosure is objected to because of the following informalities: on page 29, line 22 :"^{32}labeling of oligonucleotides", which should read "^{32}P labeling of oligonucleotides".

Appropriate correction is required.

Claim Objections

7. Claim 51 is objected to because of the following informalities: a typographical error in line 12: "… wherein at east two different regions…".

Appropriate correction is required.

8. Claims 62, 67, 68 are objected to because of the following informalities: a typographical error in line 1: "… An method…".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 51-79 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 51 is indefinite over the recitation of the limitation "electrode". Applicants do not provide a definition of a term "electrode", therefore it is not clear what is encompassed by this term. Considering the usual meaning of an electrode as a surface to which electric field can be applied, it is unclear whether the electrode claimed functions as such, since no electric field is used in the method.

B) Claims 59 and 60 recite the limitation "said blocking moiety" in line 1. There is insufficient antecedent basis for this limitation in the claims.

C) Claim 61 recites the limitation "said alkyl" in line 1. There is insufficient antecedent basis for this limitation in the claim.

D) Claims 63 and 64 recite the limitation "said blocking moieties" in line 1/2. There is insufficient antecedent basis for this limitation in the claims.

E) Claim 65 recites the limitation "said blocking moiety" in line 1. There is insufficient antecedent basis for this limitation in the claim.

F) Claim 74 recites the limitation "said blocking moiety" in line 1. There is insufficient antecedent basis for this limitation in the claim.

G) Claims 75-78 recite the limitation "said linker" in line 1. There is insufficient antecedent basis for this limitation in the claims.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Before proceeding with the rejection, definitions of terms "electrode" and "shielding" will be provided. Applicants do not define the term "electrode" in the specification. However, Applicants define "solid support comprising a metallic surface":

"... By "solid support comprising a metallic surface" or grammatical equivalents herein is meant a surface that has a metallic layer. Suitable metallic layers include any metals to which thiol groups may be attached, with gold and copper being preferred, and gold being particularly preferred. Thus, any material which can be made to contain a metallic layer or film can be used as a solid support. Accordingly, the entire surface may be metal, or only a thin layer or film of metal on the top of a different material may be used. Thus, for example, glass, plastic, polymers, graphite, or metals other than gold and copper can be used as a support, with at least a portion of one side of the support having a metallic surface.

Therefore, the term "electrode" will be considered as meaning "a solid support comprising a metallic surface". The term "shielding" is used here in its everyday meaning, i.e. "preventing physical contact". Therefore, "blocking moieties shielding nucleic acids from the electrode" means that the blocking moieties prevent contact of target and probe nucleic acids with the electrode.

13. Claims 51-58, 60-62, 64-73 and 79 are rejected under 35 U.S.C. 102(e) as being anticipated by Wohlstadter et al. (U.S. Patent No. 6,066,448).

Regarding claim 51, Wohlstadter et al. teach hybridization of target nucleic acid (analyte nucleic acid) to modified nucleic acids (nucleic acid probes) linked to a PMAMS (patterned, multi-array, multi-specific) surface, washing away unhybridized analyte and detecting the hybridization complexes with a probe specific the target nucleic acids (col. 54, lines 38-53). The PMAMS, comprising an array of binding domains, are prepared on a solid support by patterning of self-assembled monolayers. Mixed monolayers may be used to control the density of binding reagents (col. 36, lines 16-20). Binding domains contain binding reagents, such as nucleic acids (col. 11, lines 13-24, 40-50; col. 20, lines 30-67). A plurality of binding domains with different nucleic acid

probes in each of them can be prepared (col. 45, lines 56-65). The support may be metal (col. 12, lines 5-9).

Self-assembled monolayers may contain alkane thiols, which bind to gold and other metals, and the monolayer can be derivatized with the binding reagents either before or after assembly (col. 13, lines 10-30). The linker (spacer) with a formula SH-$((CH_2))_n$-Y (thiol alkane), which binds to a gold surface, can be used. The spacer is linked to a linking group, which is in turn linked to a binding reagent, which can be a nucleic acid (col. 17, lines 62-67; col. 18, lines 1-9). Detection of double-stranded oligonucleotides can be achieved using electrochemical labels which distinguish between single-stranded and double-stranded DNA, such as intercalators (col. 35, lines 13-28). To prevent non-specific binding, covalent attachment of PEG molecules may be used (col. 32, lines 9-11). Blocking molecules and blocking polymers can be covalently attached to the surface (col. 33, lines 56-64; Fig. 28). Therefore, as can be seen from Fig. 28, the blocking molecules will prevent contact of any other molecule, such as a nucleic acid, with the surface.

Regarding claims 52 and 53, Wohlstadter et al. teach attachment of binding reagents to the surface using a sulfur linkage (alkane thiol) (col. 17, lines 62-67).

Regarding claim 54, Wohlstadter et al. teach gold electrodes (col. 27, lines 21-25).

Regarding claim 55-58, 60, 61, 64, 66-68, 70-72, Wohlstadter et al. teach attachment of OH-terminated alkane thiol, SH--$(CH_2)_{11}$-OH to a gold surface, followed by addition of nucleic acids to form modified nucleic acids (col. 56, lines 14-40). Non-specific binding can be enhanced by derivatizing the surface with alkyl chains (col. 33, lines 1-3; Fig. 26, 27).

Regarding claims 65, 69 and 73, Wohlstadter et al. teach that the alkane thiols contain from 2 to 24 carbons (col. 35, lines 65-67; col. 36, lines 1-3).

Regarding claim 74, Wohlstadter et al. teach phosphate (= phosphoruc containing moiety) attachment to surfaces (col. 32, line 11).

Regarding claim 79, Wohlstadter et al. teach intercalating agents (col. 35, lines 25-28).

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 51, 52, 54, 55, 70, 72 and 74-79 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 and 15 of U.S. Patent No. 6,265,155 B1 in view of Yguerabide et al. (Anal. Biochem., vol. 228, p. 208-220, 1995).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claims. See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Independent claim 51 of the current application is drawn to a method of detecting at least one hybridization complex comprising a target nucleic acid, where the target nucleic acid is contacted with an array comprising blocking moieties and modified nucleic acids attached to an

electrode, adding an agent that distinguishes between single and double-stranded nucleic acids and detecting the hybridization complex. Claim 15 of the '155 patent differs from claim 51 in that it does not disclose detection of the presence of the hybridization complexes by addition of an agent which distinguishes between single- and double-stranded nucleic acids.

The portion of the '155 patent that supports hybridization of target nucleic acid(s) to probe nucleic acid(s) on the metallic support teaches detection of hybridization complexes by using an agent which distinguishes between single- and double-stranded nucleic acids (col. 13, lines 56-62). The '155 patent does not teach intercalating agents.

Yguerabide et al. teaches using a fluorescent intercalator (Ethidium Bromide) in the detection of DNA or RNA hybridization complexes, based on the fact that intercalators preferably bind to double-stranded nucleic acids (Abstract; page 208; page 209, paragraphs 1-4).

Therefore it would have been obvious to one of ordinary skill in the art at the time of the invention to have modified the method claim 15 of the '155 patent to include detection of hybridization complexes using an agent of Yguerabide et al. which distinguishes between single- and double-stranded nucleic acids. The motivation to do, expressly provided by Yguerabide et al., would have been that using a fluorescent intercalator provided high sensitivity, enabled use of small reaction volumes (1μL) and detection of amounts of DNA as low as 1 ng (Abstract).

Claims 2-12 of the '155 patent are drawn to the properties of the array used in the method of claim 15, and these claims correspond to dependent claims 52, 54, 55, 70, 72 and 74-78 of the current application.

16. Claims 51-64, 66-68, 70-72 and 74-79 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 and 28-33 of U.S. Patent No. 6,291,188 B1 in view of Yguerabide et al. (Anal. Biochem., vol. 228, p. 208-220, 1995).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claims. See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Independent claim 51 of the current application is drawn to a method of detecting at least one hybridization complex comprising a target nucleic acid, where the target nucleic acid is contacted with an array comprising blocking moieties and modified nucleic acids attached to an electrode, adding an agent that distinguishes between single and double-stranded nucleic acids and detecting the hybridization complex. Claim 28 of the '188 patent differs from claim 51 in that it does not disclose detection of the presence of the hybridization complexes by addition of an agent which distinguishes between single- and double-stranded nucleic acids.

The portion of the '188 patent that supports hybridization of target nucleic acid(s) to probe nucleic acid(s) on the metallic support teaches detection of hybridization complexes by using an agent which distinguishes between single- and double-stranded nucleic acids (col. 13, lines 58-64). The '188 patent does not teach intercalating agents.

Yguerabide et al. teaches using a fluorescent intercalator (Ethidium Bromide) in the detection of DNA or RNA hybridization complexes, based on the fact that intercalators preferably bind to double-stranded nucleic acids (Abstract; page 208; page 209, paragraphs 1-4).

Therefore it would have been obvious to one of ordinary skill in the art at the time of the invention to have modified the method claim 15 of the '188 patent to include detection of hybridization complexes using an agent of Yguerabide et al. which distinguishes between single-

and double-stranded nucleic acids. The motivation to do, expressly provided by Yguerabide et al., would have been that using a fluorescent intercalator provided high sensitivity, enabled use of small reaction volumes (1μL) and detection of amounts of DNA as low as 1ng (Abstract).

Claims 2-25 and 29-33 of the '158 patent are drawn to the properties of the array used in the method of claim 28, and these claims correspond to dependent claims 52-64, 66-68, 70-72 and 74-78 of the current application.

17. No references were found teaching or suggesting claims 59, 63 and 75-78, but they are rejected for other reasons.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (703) 306-5877. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

December 20, 2002

Teresa Strzelecka, Ph.D.

Patent Examiner

Teresa Strzelecka
12/20/02